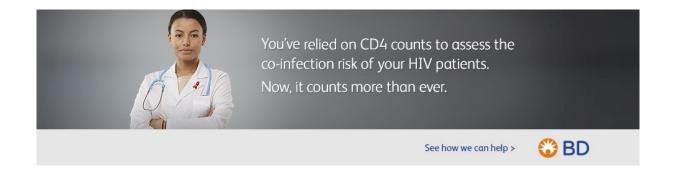
Loss of Taste and Smell as Distinguishing Symptoms of COVID-19

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Abstract

In a household study, loss of taste and/or smell was the fourth most reported symptom (26/42; 62%) among COVID-19 case-patients and had the highest positive predictive value (83%; 95% CI: 55–95%) among household contacts. Olfactory and taste dysfunctions should be considered for COVID-19 case identification and testing prioritization.

Key Words: SARS-CoV-2, COVID-19, olfactory disorders, taste disorders

Brief Report

The global coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has prompted robust public health investigations to characterize the disease course. Early published reports identified fever, cough, and shortness of breath as predominant symptoms of COVID-19 (1,2), and these classic symptoms have been used for case identification and testing prioritization. As subsequent reports described a broader range of symptoms, the Council for State and Territorial Epidemiologists (CSTE) updated its list of symptoms compatible with SARS-CoV-2 infection in March 2020 (3), adding loss of taste and smell. Although several reports have described these newly recognized symptoms of loss of taste and smell among individuals diagnosed with COVID-19 (4-6), few studies have prospectively evaluated these symptoms among close contacts of COVID-19 cases prior to diagnosis and outside of a clinical setting.

CDC, in partnership with Wisconsin Department of Health Services and local health departments, conducted a household study that included known COVID-19 index cases and their household members. This investigation provided an opportunity to identify household COVID-19 cases and describe their symptom profiles, including loss of taste and smell, prior to diagnosis.

Methods

All activities in this investigation were part of the public health response and determined as not human subjects research. During March–April 2020, health department personnel in Milwaukee County, Wisconsin, assisted CDC in identifying a convenience sample of households with a laboratory-confirmed COVID-19 index case ≤10 days from diagnosis who resided in the

home at enrollment and lived with at least one other household member. Informed consent was obtained for all participants. All participants completed questionnaires assessing basic demographic information, medical history, symptoms since the index case's disease onset, and other epidemiological information. A parent or legal guardian assisted in completing questionnaires for children <18 years. At enrollment, we collected nasopharyngeal (NP) swabs from all participants; to fulfill a secondary objective of this investigation, we also collected nasal self-collect (NSC) swabs from index cases and symptomatic household members.

The City of Milwaukee Health Department Laboratory tested swabs using the CDC SARS-CoV-2 real-time reverse transcription polymerase chain reaction (RT-PCR) assay (7). We classified any participant having a SARS-CoV-2—positive NP swab or NSC swab collected in the 10 days prior to and including enrollment as a COVID-19 case.

We compared the prevalence of symptoms among cases descriptively and computed bivariate analyses of demographic, medical history, and symptoms with reported loss of taste and/or smell using two-tailed Pearson's chi-squared test or Fisher's exact test. We calculated the positive predictive value and 95% CIs of individual symptoms for COVID-19 among household contacts. Statistical analyses were performed using SAS® Version 9.4, SAS Institute Inc., Cary, North Carolina.

Results

We enrolled 90 participants from 26 households, including 26 index cases and 64 household members. Overall, 48 (53%) study participants were male; 69 (77%) were adults ≥18 years old (median=31 years; range: <1–90 years); 41 (46%) were black non-Hispanic/Latino, 37 (41%) were white non-Hispanic/Latino, and 12 (13%) were other races/ethnicities. Preexisting

medical conditions were reported by 39 (43%) participants, including asthma or reactive airway disease (n=13), hypertension (n=10), and diabetes (n=8). Upon enrollment, 16/64 (25%) household contacts tested positive for SARS-CoV-2 (including two who were positive by NSC only), totaling 42/90 (47%) COVID-19 cases. The median age of household contacts who tested positive was 21 years [interquartile range (IQR): 16–50], compared to 23 years (IQR: 12–48) for household contacts who tested negative. Median time from symptom onset to enrollment for index cases and symptomatic household cases was 14.5 days (IQR: 10.0–19.0) and 7.0 days (IQR: 5.0–7.5), respectively.

Among the 42 individuals with laboratory-confirmed SARS-CoV-2, all (100%) reported at least one symptom (**Table 1**); 38 (90%) reported at least one classic COVID-19 symptom. The most frequently reported symptoms were cough (81%), headache (76%), fever (subjective or measured \geq 100.4°F) (64%), loss of taste and/or smell (62%), and nasal congestion (62%).

Among the 26 participants with COVID-19 who reported loss of taste and/or smell, 24 reported loss of taste with 14/24 (58%) reporting complete loss; 18 participants reported loss of smell with 13/18 (72%) reporting complete loss. There were no significant differences in reporting loss of taste and/or smell by sex, age <18 years versus ≥18 years, race/ethnicity, presence of medical conditions, or between index and household member cases (all p>0.05). Of the 26 participants reporting any loss of taste and/or smell, 9 (35%) reported it in the absence of nasal congestion. Participants with COVID-19 reporting loss of taste and/or smell were more likely to report headache (88% vs. 56%; p=0.03) but were no more or less likely to report any other symptom (p>0.05). No participant reported loss of taste and/or smell as the only symptom. When loss of taste and/or smell was added to the classic symptoms, 95% of participants with

COVID-19 reported at least one of loss of taste and/or smell, fever, cough, and shortness of breath.

Among the 64 household members of COVID-19 index cases, loss of taste and/or smell was reported by 12 individuals, of whom 10 were positive for SARS-CoV-2. The positive predictive value (PPV) of any loss of taste and/or smell (83%, 95% CI: 55–95%) was higher than for fever (subjective or measured) and cough, two of the three classic symptoms, and equal to the third, shortness of breath (83%, 95% CI: 44–97%) (**Table 1**). The PPV for complete loss of taste and/or smell (86%, 95% CI: 49–97%) was the highest among any of the symptoms.

Discussion

In this household-based population of individuals with COVID-19, including mildly symptomatic individuals who otherwise may not have been tested according to contemporaneous public health guidance (8), loss of taste and/or smell was reported by more than three of every five individuals with confirmed COVID-19. Among the 64 household contacts of COVID-19 index cases, it had the highest PPV of all symptoms, matched only by shortness of breath. When compared to other symptoms, loss of taste and/or smell appeared highly predictive of SARS-CoV-2 infection and was more predictive than cough.

Nasal congestion alone is unlikely to explain the taste and smell alterations, as one-third of patients reporting loss of taste and/or smell did not report nasal congestion; other analyses have shown an even smaller proportion of COVID-19 cases with concurrent nasal congestion (9). Investigations into the mechanism of COVID-19-related olfactory and taste dysfunction include demonstration of olfactory nerve infection by SARS-CoV, the virus that causes SARS, and expression of angiotensin converting enzyme 2 (ACE2), the receptor involved in SARS-

CoV-2 pathogenesis, on olfactory epithelial cells in animal models (5,10). Studies in human models have shown broad expression of ACE2 on the epithelial cells of the tongue and oral cavity mucosa (11,12). The underlying mechanism for these symptoms is an area of active investigation.

This analysis is subject to limitations. All symptoms and medical histories were self-reported and limited by patient recall, health literacy, and availability of home thermometers. Because prior and current symptom ascertainment and SARS-CoV-2 testing were conducted at enrollment, any subsequent development of symptoms or infection that could affect PPVs were not captured, and timelines for pre-enrollment symptoms are not available. However, this approach likely reduced selection biases that may be present in other reports describing the association between loss of taste and smell with SARS-CoV-2 infection. Due to the high prevalence (25%) of COVID-19 infection within this population, the PPV identified in this analysis may not be representative of all clinical encounters. However, our findings may be particularly relevant for screening individuals in close contact with known cases. Finally, the sample size was small, resulting in wide overlapping confidence intervals for the reported PPVs.

In this investigation, adding loss of taste and/or smell to the classic clinical criteria would have captured 95% of cases while only misidentifying two non-cases as cases, compared to 14 non-cases that would have been misidentified by the classic symptoms. In the absence of confirmatory laboratory testing, CSTE criteria for a probable COVID-19 case now include loss of taste and/or smell in conjunction with other non-classic symptoms (3). Our findings suggest that adding loss of taste and/or smell to the singular CSTE clinical criteria, which currently include cough, shortness of breath, and difficulty breathing, may increase the efficiency of probable COVID-19 case identification.

Due to limited testing capacity, most states have prioritized testing of moderately to severely ill patients. However, as the availability of contact tracing and testing expands, testing and diagnoses will shift to include outpatients with milder illness. Identifying these cases will assist in appropriate isolation recommendations and the prevention of additional spread within the community. Clinicians will benefit from further characterization of the full spectrum of illness in patients and may consider using loss of taste and/or smell in their testing strategies.

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Table 1. Prevalence of self-reported symptoms among individuals with and without laboratory-confirmed COVID-19, and positive predictive value (PPV) of self-reported symptoms prior to testing among household contacts of COVID-19 index cases, Milwaukee County, Wisconsin, March–April 2020.

		Household Household					
		Household	Contact	Contact	Symptom PPV among		
	All Cases	Index Cases	Cases	Non-Cases	Household Contacts		
Symptom	(N=42)	(N=26)	(N=16)	(N=48)	(N=64)		
		n (º	%)		% (95% CI)		
Classic COVID-19 symptoms (any)	38 (90%)	24 (92%)	14 (88%)	14 (29%)	50% (33–67%)		
Cough	34 (81%)	22 (85%)	12 (75%)	13 (27%)	48% (30–67%)		
Fever (any)	27 (64%)	18 (69%)	9 (56%)	3 (06%)	75% (47–91%)		
Measured fever ≥100.4°F	14 (33%)	11 (42%)	3 (19%)	1 (02%)	75% (30–95%)		
Subjective fever	26 (62%)	18 (69%)	8 (50%)	2 (04%)	80% (49–94%)		
Shortness of breath	19 (45%)	14 (54%)	5 (31%)	1 (02%)	83% (44–97%)		
Other symptoms (any)	41 (98%)	25 (96%)	16 (100%)	29 (60%)	36% (23–50%)		
Headache	32 (76%)	18 (69%)	14 (88%)	16 (33%)	47% (30–64%)		

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Loss of taste or smell (any)	26 (62%)	16 (62%)	10 (63%)	2 (04%)	83% (55–95%)
Loss of taste (any)	24 (57%)	16 (62%)	8 (50%)	2 (04%)	80% (49–94%)
Loss of smell (any)	18 (43%)	10 (38%)	8 (50%)	1 (02%)	89% (57–98%)
Complete loss of taste or smell	16 (38%)	10 (38%)	6 (38%)	1 (02%)	86% (49–97%)
Complete loss of taste	14 (33%)	9 (35%)	5 (31%)	1 (02%)	83% (44–97%)
Complete loss of smell	13 (31%)	7 (27%)	6 (38%)	1 (02%)	86% (49–97%)
Nasal congestion	26 (62%)	14 (54%)	12 (75%)	9 (19%)	57% (37–76%)
Myalgia	24 (57%)	16 (62%)	8 (50%)	3 (06%)	73% (43–90%)
Chills	23 (55%)	18 (69%)	5 (31%)	3 (06%)	63% (31–86%)
Rhinorrhea	20 (48%)	12 (46%)	8 (50%)	13 (27%)	38% (21–59%)
Sore throat	18 (43%)	11 (42%)	7 (44%)	10 (21%)	41% (22–64%)
Fatigue*	15 (36%)	10 (38%)	5 (31%)	6 (13%)	NR [‡]
Nausea/vomiting	12 (29%)	10 (38%)	2 (13%)	1 (02%)	67% (21–94%)
Diarrhea	11 (26%)	8 (31%)	3 (19%)	10 (21%)	23% (08–50%)
Abdominal pain	10 (24%)	6 (23%)	4 (25%)	4 (08%)	50% (22–78%)
Chest pain/discomfort*	8 (19%)	4 (15%)	4 (25%)	2 (04%)	NR [‡]

Lightheadedness*	3 (07%)	2 (08%)	1 (06%)	0 (00%)	NR [‡]
Loss of appetite*	3 (07%)	3 (12%)	0 (00%)	2 (04%)	NR [‡]
Wheezing*	3 (07%)	2 (08%)	1 (06%)	0 (00%)	NR [‡]
Other* [†]	5 (12%)	5 (19%)	0 (00%)	NR [§]	NR [‡]

^{*}Not included in list of symptoms, but self-reported in "other" category.

[†]Includes single reports each of difficulty focusing, dry eyes, eye pain, hives, nasal pain, and photosensitivity.

[‡]Positive predictive value not reported because symptom was reported in the "other" category and was not systematically evaluated among all participants.

[§]Values not reported for single reports of other symptoms among those who tested SARS-CoV-2–negative (i.e., non-cases).